

Case Reports

A case of chronic granulomatous disease

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Sri Lanka Journal of Child Health, 2000; **29**: 27-28

(Key words: Chronic granulomatous disease; phagocyte deficiencies)

Introduction

Chronic granulomatous disease (CGD) is an inherited disorder in which phagocytes are unable to generate reactive oxygen intermediates, such as superoxide, due to defects in gene coding for one of several components of the NADPH oxidase. Patients develop severe, recurrent infections with catalase-positive bacteria and fungi¹. Frequently, CGD is inherited as an X-linked recessive disease associated with cytochrome b₅₅₉ deficiency². Affected patients have recurrent infections from infancy, usually involving the skin, lymph nodes, lungs, liver and gastrointestinal tract. These bacterial and fungal infections are responsible for early deaths³.

Case report

A one year and ten month old baby from Mannar was admitted to the Anuradhapura General Hospital in May 1999 with unresolving pneumonia. Whilst being treated there, the child developed a pneumothorax and was transferred to the cardio-thoracic unit of the National Hospital, Colombo for intercostal drainage. In June 1999, the child was transferred to the Lady Ridgeway Hospital (LRH) for further investigation.

On admission to LRH, the child had fever, cough and shortness of breath for over 2 months, accompanied by loss of weight and loss of appetite. There was no consanguinity. Two male siblings had died after developing pneumonia, one at the age of 3 months and the other at the age of 5 years.

On examination, the child was febrile and wasted with oral ulcers, hepato-splenomegaly and clubbing. There was no lymphadenopathy. There were bilateral crepitations over the lungs. Chest x-ray showed bilateral pneumatoceles. After 2 weeks of therapy with ceftriaxone, cloxacillin and netilmycin, there was marked improvement in the clinical signs and chest x-ray.

The ESR was 133 mm in the first hour and the haemoglobin was 9.4 g/dl. The total white cell count was $10.4 \times 10^9/L$ (N 59%, L 36%, E 4%, M 1%). The peripheral blood film showed a moderate neutrophil leucocytosis and a hypochromic, microcytic anaemia. Serum immunoglobulin levels were as follows - IgG 2378 mg/dl (normal range 258-1393), IgA 200 mg/dl (normal range 19-119), IgM 290 mg/dl (normal range 14-114). Neutrophils from the patient did not exhibit dye reduction with the nitroblue tetrazolium (NBT) test. However, the myeloperoxidase activity of neutrophils was normal. Based on these findings, a diagnosis of chronic granulomatous disease (CGD) was made and the child was started on long term cotrimoxazole prophylaxis. This is the first laboratory confirmed case of CGD in Sri Lanka.

Discussion

Reduction of nitroblue tetrazolium (NBT) dye is the standard method for detecting defective oxidative metabolism and making the diagnosis of CGD⁴. Phagocytes from patients with CGD fail to generate any superoxide anion during phagocytosis and are unable to reduce NBT. Neutrophil leucocytosis, hypochromic microcytic anaemia, elevated ESR and increased serum immunoglobulin concentrations found in our patient merely reflect response to chronic infection. The most common catalase-positive organism causing infection in CGD is *Staphylococcus aureus* which accounts for about 40% of clinical infection isolates. Other catalase-positive organisms include *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Serratia marescens*, *Salmonella* and *Pseudomonas* species which account for an additional 30% of infections. Yeast and fungi, particularly *Aspergillus*, account for another 30% of isolates³. Bacterial prophylaxis with a daily anti-staphylococcal agent has been demonstrated to reduce significantly the incidence of bacterial infections⁵. Common catalase-negative organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae* do not usually cause problems because they release into phagocytic vacuoles small amounts

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of hydrogen peroxide that is used by the CGD phagocyte to kill these bacteria.

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